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EXAMINER	
YU, MELANIE J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,140	SEM ET AL.	
	Examiner	Art Unit	
	Melanie Yu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8 July 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14, 16, and 18-49* is/are rejected.

7)☒ Claim(s) *15 and 17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 May 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/8/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Priority

1. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application, 60/258,621 (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application, and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-10 and 33-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In part (c) of claim 1, it is the term "demagnetizes" is vague and indefinite because it is unclear if the pulse sequence demagnetizes the protons of the macromolecule or whether the protons of the macromolecule are still magnetized with a different magnetization than that of the second proton.

3. Claim 6 recites the limitation "the polypeptide" in the second line. There is insufficient antecedent basis for this limitation in the claim. No polypeptide has been specified in claim 1, the claim should be dependent on claim 2.

Claims 7-10 recite the limitation "the amino acids of the protein" in the second line of each claim. No proteins or amino acids were specified for assignation in claim 1.

With respect to part (b) of claims 33, 38, and 44, it is unclear whether the second molecule is also the ligand bound to the macromolecule.

With respect to claims 38-49, the term "alternatively" is vague and indefinite because it is unclear if it is meant that the second molecule and second ligand associate with the macromolecule at the same time or at the same place on the macromolecule.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1, 2, 6, 13, 14, 18-25, 27-29, and 32-49 are rejected under 35 U.S.C. 102(e) as being anticipated by Sem (US patent 6,333,149)

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Sem teaches a method for preferentially observing an exposed position of a macromolecule, comprising the steps of (a) obtaining a sample comprising a macromolecule, being an enzyme, 1 (Fig. 1a, col. 3, lines 66-67; col. 4, lines 1-67) and a second molecule 2,3 (Fig. 1b; col. 2, lines 29-31; col. 5, lines 1-27), wherein the macromolecule is an enzyme larger than 150 kDa, which is encompassed by the recited larger than about 35 kDa, larger than about 50 kDa, larger than about 75 kDa, and larger than about 100 kDa (col. 4, lines 6-8), wherein a first proton is bound to the exposed position, 3 (Fig. 1b; col. 1, lines 51-55) of the macromolecule, a second proton bound to the second molecule, and the first proton can exchange with the second proton; (b) applying a magnetic field to the sample (col. 8, lines 55-67; col. 9, lines 1-10); (c) irradiating the sample with a radiofrequency, which is a pulse sequence because irradiation occurs at frequencies other than at the resonant frequency (col. 8, lines 1-5) and the radio frequency further comprising ^{15}N, ^{1}H TROSY (col. 17, lines 15-25) ; (d) allowing the second proton to exchange with the first proton (col. 6, lines 26-29; col. 6, lines 66-67; col. 7, lines 1-8); (e) detecting the magnetization from the second proton (col. 8, lines 12-16; col. 9, lines 21-24). The enzyme identified by NMR, by Sem, is encompassed by the identification of the recited polypeptide. Sem uses the NMR method to identify NMR cross-peaks corresponding to the perturbed atoms, which requires detection of magnetization (col. 10, lines 29-32); (f) determining a heteronuclear correlation measurement for the sample, wherein the correlation measurement is an ^{15}N–^{1}H correlation measurement (col. 9, lines 24-30); and (g) determining a second heteronuclear correlation between the correlated nuclei and a third nucleus (col. 15, lines 30-42) by displacing a common ligand and binding a common ligand mimic and detection by

incorporating a HNCA measurement (col. 17, lines 38-48). Sem also teaches incorporating a NOESY measurement (col. 3, lines 1-2; col. 9, lines 33-37; col. 17, lines 35-54).

With respect to claims 13 and 14, Sem teaches the position on the macromolecule that is exposed to the second molecule comprising ^{15}N and the pulse sequence comprising an ^{15}N filter (col. 7, lines 2-8; col. 9, lines 30-43; col. 10, lines 58-60).

With respect to claims 28-32, Sem teaches a macromolecule having a ligand bound to a position other than the exposed position 2, Fig. 1B (col. 1, lines 55-60; col. 6, lines 13-26) and the second molecule of the method being a ligand (col. 1, lines 51-55; col. 2, lines 29-32), wherein the ligand is a natural ligand or a mimic of a natural ligand (col. 5, lines 47-49).

With respect to claims 33-38, 40-44, and 46-49, Sem teaches a method for observing a position in a macromolecule that is differentially exposed to two ligands (a common ligand and a mimic common ligand), wherein the macromolecule is larger than 35 kDa and has a plurality of protons bound to positions on the macromolecule that are exposed to a second molecule (col. 9, lines 45-50), comprising the steps of: a) performing the method for preferentially observing an exposed position of a macromolecule, as disclosed above, to a first sample comprising the macromolecule (protein; 1, Fig. 4B), the second molecule (common ligand, 4, Fig. 4B) and a first ligand (mimic common ligand; 4, Fig. 4A), wherein the second molecule and first ligand alternatively associate with and dissociate from the macromolecule at site 1b in Fig. 4B (col. 7, lines 61-67; col. 8, lines 1-7); b) performing the method of claim 1 to a second sample comprising the macromolecule (protein; 1, Fig. 4B), the second molecule (common ligand, 4, Fig. 4B) and a second ligand (mimic common ligand; 5, Fig. 4A), wherein the second molecule and the second ligand alternatively associate with and dissociate from the macromolecule (col. 7,

lines 61-67; col. 8, lines 1-7); and c) detecting a perturbation being a chemical shift change, reduced signal intensity, or differential proton exchange between the first and second sample (col. 9, lines 14-16) and comparing the perturbation in the second sample to the first sample (col. 16, lines 51-65; col. 17, lines 37-67; col. 19, lines 1-3). Sem also teaches a second ligand bound to the macromolecule in the first sample in a position other than the binding position of the first ligand (specific ligand; 8, Fig. B; col. 3, lines 5-7).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 1-6, 13, 14, 18-25, 27, 29, and 33-35 are rejected under 35 U.S.C. 102(b) as anticipated by Fesik et al. (US patent 5,804,390) in light of Bax et al. (Methodological Advances in Protein NMR, Acc. Chem. Res., 1993) or, in the alternative, under 35 U.S.C. 103(a) as obvious over Fesik et al. in view of Bax et al.

9. Fesik et al. teach a screening process of a 45 kDa macromolecule (col. 12, lines 3-5) with the generation of a 2-dimensional $^{15}N/^{1}H$ correlation spectrum, but fail to disclose the detailed steps of the process, and reference Bax et al. as the method used for generation of a 2-D $^{15}N/^{1}H$ correlation spectrum.

Bax et al., as referenced by Fesik et al., teach two-dimensional NMR steps comprising: a sample comprising a macromolecule and a second molecule (Figure 2, sample comprises macromolecule, staphylococcal, and a second molecule, amide protons); when a sample is placed in a NMR spectrometer, a magnetic field is applied to the sample in order to magnetize the protons of the sample; irradiating the sample with a pulse sequence that demagnetizes the protons of the macromolecule relative to the second proton (pg. 132, left column, 2nd paragraph, 4th and 5th sentence); allowing the second proton to exchange with the first proton, whereby the relatively magnetized second proton becomes bound to the exposed position (pg. 132, left column, 2nd paragraph, 3rd sentence); and detecting the magnetization from the second proton (pg. 132, left column, 2nd paragraph, last sentence), in order to structurally characterize biopolymers using 2-D and 3-D NMR.

Therefore it would have been obvious to include in the method of Fesik et al., the 2D NMR method as taught by Bax et al. and referenced by Fesik et al., in order to generate two-dimensional $^{15}N/^{1}H$ correlation spectrum in the screening process.

With respect to claims 2 and 29, Fesik et al. teach the macromolecule being a polypeptide (col. 7, lines 1-4) and the second molecule being a ligand (col. 2, lines 33-35)

With respect to claims 3-5, Fesik et al. teach the macromolecule being 45 kDa, which encompasses the recited greater than 35 kDa of claim 1. Fesik et al. also teach the

macromolecule being larger than about 50 kDa, about 75 kDa, or about 100 kDa (col. 8, lines 7-9). Furthermore, Fesik et al. state the method can be used for target molecules being polypeptides with a high resolution NMR spectrum that can be partially or uniformly labeled with ^{15}N (col. 7, lines 8-10). Therefore the method taught by Fesik et al. would be useful for any polypeptide regardless of molecular weight, and it would have been obvious to one having ordinary skill in the art at the time the invention was made to generate a $^{15}N/^{1}H$ correlation spectra using any ^{15}N-labeled polypeptide that gives high resolution NMR spectrum.

With respect to claim 6, Fesik et al. teach using the two-dimensional $^{15}N/^{1}H$ NMR correlation spectroscopic screening process as method as disclosed by Bax et al. to determine part of a structure of a polypeptide (col. 3, lines 46-55).

With respect to claims 13 and 14, Fesik et al. teach the position on the macromolecule that is exposed to the second molecule comprising ^{15}N (col. 7, lines 14-20), and the pulse sequence comprising a ^{15}N filter (col. 15, lines 44-46). Fesik et al. teach the complex points using sweep widths of 2000 Hz at ^{15}N for the time period of t_1, which indicates a ^{15}N filter.

With respect to claims 18-21, Fesik et al. teach a mixing time of 80 ms (col. 22, lines 66-67), which is encompassed by the recited between 25 and 300 ms, the between 50 and 150 ms, and the between 80 and 120 ms.

With respect to claims 22-25 and 27, Fesik et al. teach determining a heteronuclear correlation measurement wherein one of the correlated nuclei is ^{1}H and the correlation measurement is a ^{15}N-^{1}H correlation measurement (col. 2, lines 35-47), and further determining a second heteronuclear correlation measurement between the correlated nuclei and a third nucleus (col. 21, lines 15-26). In order to conduct a ^{15}N-^{1}H correlation measurement, one of the

correlated nuclei must be ^{1}H. The third nucleus is incorporated into the second step of the process of Fesik et al. wherein the screening process is performed in order to identify the second ligand. Fesik et al. also teach incorporating a HNCA (col. 21, lines 38-45) a NOESY (col. 21, lines 61-66) measurement.

With respect to claims 28 and 32, Fesik et al. teach the macromolecule having a ligand bound to a position other than the exposed position (col. 10, lines 52-56; col. 11, lines 10-18). Fesik et al. also teaches the sample in a solvent, further comprising the step of irradiating the sample with a pulse sequence that preferentially demagnetizes the protons of the solvent (col. 23, lines 12-23).

With respect to claims 30 and 31, Fesik et al. teach the second molecule being a ligand that can bind to the target molecule (col. 5, lines 52-67). The natural and mimic ligands as recited by the instant claims have the same function to bind to an exposed portion of the macromolecule. The ligands taught by Fesik et al. also have the ability to bind to a macromolecule. Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to include any natural or mimic ligands having the ability to bind to a macromolecule in the method of Fesik et al.

With respect to claims 33-49, Fesik et al. teach a sample wherein a macromolecule that binds a ligand is larger than 35 kDa (col. 12, lines 3-5); has a plurality of protons bound to positions that are exposed to a second molecule, and are exposed to a second molecule; and the exposed protons can exchange with protons of the second molecule; the method comprising the steps of: performing the method of Bax et al., as disclosed above, to a first sample comprising the macromolecule and a second molecule and a first ligand (col. 2, lines 36-39); performing the

method of Bax et al. as disclosed above to a second sample comprising the macromolecule, the second molecule, and a second ligand, wherein the second molecule and second ligand alternatively associate and dissociate from the macromolecule (col. 2, lines 39-42); and detecting a perturbation of a chemical shift change (col. 2, lines 42-47 and 66-67) in the second sample compared to the first sample. Fesik et al. teach the perturbation alternatively being a change in signal intensity (col. 7, lines 37-40) or a differential proton exchange between the first and second sample (col. 23, lines 61-66).

Claims 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fesik et al. in view of Bax et al.

Fesik et al. in view of Bax et al., as disclosed above, teach generating a $^{15}N/^{1}H$ NMR correlation spectrum of the macromolecule.

Fesik et al. teach assignation of amino acids of a protein by an NMR technique, but fail to teach the exact amounts of fewer than 5%, fewer than 10%, fewer than 50%, and fewer than 75% of the amino acids assigned by NMR techniques. Nevertheless, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering an optimum value of a result effective variable involves only routine skill in the art. *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value for a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation" Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges

of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since applicant has not disclosed that the specific limitations recited in instant claim 13 are for any particular purpose or solve any stated problem, and the prior art teaches that the amount of components in a solution and the parameters of a solution can be varied according to the sample being analyzed, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the prior art by normal optimization procedures known in the art of detecting and identifying amino acids.

10. Claims 12 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fesik et al. in view of Bax et al. further in view of Ohno et al. (NMR Structure of the Streptomyces Metalloproteinase Inhibitor, SMPI, Isolated from Streptomyces nigrescens TK-23. J. Mol. Biol. Vol. 282. 1998, 421-423).

With respect to claim 26, Fesik et al. in view of Bax et al., as disclosed above, teach a method of observing an exposed position of a macromolecule, but fail to teach incorporating a HNCACB measurement.

Ohno et al. teach a resonance experiment of HNCACB in order to carry out sequence-specific backbone NMR signal experiments (pg. 422, last paragraph).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Fesik et al. in view of Bax et al., a HNCACB measurement as taught by Ohno et al., as an alternative heteronuclear correlation measurement.

With respect to claim 12, Ohno et al. teach the second molecule being water (pg. 422, last paragraph).

11. Claim 11 is rejected under 35 U.S.C 103(a) as being unpatentable over Fesik et al. in view of Bax et al. further in view of Xu et al. (*J. Am. Chem. Soc.* 1996, 118:9176-9177).

Fesik et al. in view of Bax et al., as disclosed above, teach a method for observing an exposed position of a macromolecule, but fail to teach the second molecule being a protic solvent.

Xu et al. teach a second molecule being a protic solvent in order to act as a catalyst to lower the potential energy barrier between conformation states (pg. 9176, 1st paragraph).

Therefore, it would have been obvious to one having ordinary skill in the art to include in the method of Fesik et al. in view of Bax et al., a protic solvent as the second molecule as taught by Xu et al., in order to destabilize electrostatic interactions in macromolecular structures and induce dynamics in order to stabilize complex formation for a clear NMR chemical shift analysis.

12. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fesik et al. in view of Bax et al. further in view of Pervushin et al. (U.S. patent 6,133,736).

Fesik et al. in view of Bax et al., as disclosed above, teach the method for preferentially observing an exposed position of a macromolecule, but fail to teach the irradiation step further comprising $^{15}N,^{1}H$ TROSY.

Pervushin et al. teach $^{15}N,^{1}H$ TROSY in order to significantly reduce transverse relaxation rates and overcome key obstacle opposing solution NMR of larger molecules (col. 1, lines 31-36; col. 2, lines 16-21).

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Fesik et al., a $^{15}N,^{1}H$ TROSY measurement as taught by Pervushin et al., in order to optimize NMR experiments for resonance assignments and collection of conformational constraints of large molecules and to provide a better ratio of signal height to noise.

13. Claims 39 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sem et al. (US patent 6,333,149). Sem et al. teach a method for observing a position in a macromolecule that is differentially exposed to two ligands, but fails to teach the rate at which the ligand associates with the macromolecule as slower than or at most 10 fold higher than the rate at which the exposed protons of the macromolecule exchange with protons of the second molecule.

However, since no further steps are taken to affect the rate at which the ligand associates with the macromolecule, it would have been obvious to one having ordinary skill in the art at the time the invention was made that the ligand and the macromolecule would associate slower than or at most 10 fold higher than the rate at which the exposed protons of the macromolecule exchange with protons of the second molecule.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 13, 22-25, 27-31, and 33-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 13, and 25-31 of U.S. Patent No. 6,333,149. Although the conflicting claims are not identical, they are not patentably distinct from each other because the same method is recited with different terms.

The patent '149 recites a method in the claims that one of ordinary skill in the art would recognize that those would encompass the method recited in the instant claims. While patent '149 recites the usage of NMR, it fails to recite applying a magnetic field to the sample, thereby magnetizing the first proton and the second proton. However, Claim 1 of the patent '149 recites the step of identifying in a multidimensional NMR experiment, an NMR cross-peak corresponding to a nucleus (step (a), 3), which would inherently include the step of applying a magnetic field as recited in the instant claims (also see specification; col. 8, lines 45-62). Furthermore, the patent fails to recite allowing the second proton to exchange with the first proton, however claim 1 of the patent recites a method for identifying an atom (proton) of a

common ligand mimic that is proximal to an interface region of an enzyme. In order for the atom (proton) to be proximal to the interface region, the atom (proton) must exchange with the atom on the enzyme. Furthermore, the term "atom" encompasses a proton as defined by the specifications of the patent (col. 6, lines 26-29).

The specific limitations recited by dependent claims 7, 8, and 25-31, of the patent, would be recognized by one of ordinary skill in the art as encompassed by the dependent claims, 2-6, 13, 22-25, 27-31, and 33-37, recited by the application.

15. Claims 1-6, 13, 22-25, 27-31, and 33-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2, 8, 14-46, 34, 36, 37, 40, 43, 44, and 46 of U.S. Patent No. 6,620,589. Although the conflicting claims are not identical, they are not patentably distinct from each other because the same method is recited with different terms.

With respect to claims 1 and 29-31, the patent recites a method that one of ordinary skill in the art would recognize as encompassing the method recited in the instant claims. While the patent '589 recites the usage of NMR, it fails to recite applying a magnetic field to the sample, thereby magnetizing the first proton and the second proton. However, Claim 2 of the patent '589 recites the step of identifying in a multidimensional NMR experiment, an NMR cross-peak corresponding to a nucleus (step (a), 3), which would inherently include the step of applying a magnetic field as recited in the instant claims (also see specification; col. 10, lines 30-47). The patent also fails to recite the step of allowing the second proton to exchange with the first proton is not specifically recited in the claims of the patent, however claim 1 recites a method for identifying an atom (proton) of a common ligand mimic that is proximal to an interface region of

an enzyme. In order for the atom (proton) to be proximal to the interface region, the atom (proton) must exchange with the atom on the enzyme. Furthermore, the term "atom" encompasses a proton as defined by the specifications of the patent (col. 7, lines 64-67).

The specific limitations recited by dependent claims 14-16, 34, 36, 37, 40, 43, 44, and 46 of the patent, are encompassed by the dependent claims 2-6, 13, 22-25, 27-31, and 33-37 of the application.

Allowable Subject Matter

16. Claims 15 and 17 are allowed.

17. The following is a statement of reasons for the indication of allowable subject matter: The following is an examiner's statement of reasons for allowance: the prior art fails to teach to a method of irradiating with the SEA pulse sequence or the SEA-TROSY pulse sequence.

18. Claims 15 and 17 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

19. Claims 15 and 17 are free of the prior art.

20. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Maryanskl et al. (US patent 5,633,584) teach detection and imaging of the energy field of a proton exchange between hydration layers and water.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melanie Yu whose telephone number is (571) 272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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